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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/546,829	08/25/2005	Yoichi Taya		1022

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EXAMINER	
GUSSOW, ANNE	
ART UNIT	**PAPER NUMBER**
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/546,829	TAYA ET AL.	
	Examiner	Art Unit	
	Anne M. Gussow	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 August 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of: ,

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *Sept. 1, 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 2-4 and 6-7 have been cancelled.

2. Claims 1 and 5 are under examination.

Specification

3. The disclosure is objected to because of the following informalities: there are grammatical and typographical errors in the specification, for example, on page 2 line 6 "solving above described purpose" should read "solving the above described purpose" and on page 5 line 25 "to" should read "into".

Appropriate correction is required throughout.

Claim Objections

4. Claims 1 and 5 are objected to because of the following informalities: the claims contain grammatical errors. The phrase "substituted to phenylalanine" should read "substituted with phenylalanine".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a.) Claim 1 is indefinite for reciting "comprising a transcriptional factor as an effective component, which comprises p53 or mutated p53". It is not clear if the transcriptional factor is the effective component of if the p53 or mutated p53 is the effective component.

b.) Claim 5 is indefinite for reciting "injecting a transcriptional factor, which comprises p53 or a mutated type p53 wherein said serine residue at amino acid position 46 is substituted to phenylalanine and clathrin heavy chains to a cancer cell, or injecting clathrin heavy chains to a cancer cell". It is not clear what the method is, are p53 or mutated p53 and clathrin heavy chains being injected into the cancer cell or are just the clathrin heavy chains being injected into the cancer cells?

c.) Claims 1 and 5 recite the limitation "said serine residue" in line 4 of the claim. There is insufficient antecedent basis for this limitation in the claim.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1 and 5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988).

> Wands states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn to a cancer treatment drug comprising a transcriptional factor component of p53 or mutated p53, which contains a serine residue at position 46 substituted with phenylalanine, and clathrin heavy chains and a method for treating just any cancer with the drug.

The specification teaches transfecting cells *in vitro* with mutated p53, which contains a serine residue at position 46 substituted with phenylalanine and measuring an increase in the expression of a p53AIP1 reporter plasmid (example 1 page 10 and figure 9). Applicants have not provided any direction or guidance to assist one skilled in the art in the treatment of cancer with a drug comprising a transcriptional factor component of p53 or mutated p53 and clathrin heavy chains. Further, the as-filed specification fails to address the following issues:

1.) is cell death induced by the composition of p53 and clathrin heavy chains

2.) what cancer types would be affected by the treatment

3.) is the treatment effective *in vitro* or *in vivo*

4.) what is an effective treatment dose

The goal of treating cancer is to eliminate the cancerous cells. It is well known in the art that p53 is a tumor suppressor gene required for anti-cancer drug-induced apoptosis. Cancer cells with a mutant p53 gene loose the ability to arrest at G_0/G_1 or G_2/M and the cell cycle cannot be stopped, resulting in resistance to apoptosis (Kim, et al. 2003, Anti-Cancer Drugs, Vol. 14 pages 3-11). Kim, et al. teach introduction of the p53 gene into cancer cells via an adenovirus vector is not sufficient to decrease tumor volume (page 5, middle of 2nd column). Ferreira, et al. (Annals of Oncology, 1999, Vol. 10 pages 1011-1021) teach in some systems inactivation of p53 results in increased resistance, while in other cases disruption of wild type p53 function relates to increased drug sensitivity (page 1014, preclinical data).

Additionally, Zips, et al. (in vivo, 2005, Vol. 19 pages 1-8) teach that both functional and non-functional assays (page 1 bottom of 2nd column to page 2 top of 1st column) and in vitro and in vivo studies with more than one tumor cell line (page 6, conclusion) are each a necessary component of assessing new anti-cancer agents. Thus, there is insufficient evidence that would lead the skilled artisan to predict the ability to treat cancer with wild type or mutant p53 and clathrin heavy chains. The specification does not teach how wild type or mutant p53 and clathrin heavy chains would kill cancer cells.

In view of the lack of predictability of the art to which the invention pertains and the lack of established protocols for treating just any cancer with a wild type or mutant p53 and clathrin heavy chains undue experimentation would be required to practice the claimed invention with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed invention and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for treating cancer, commensurate in scope with the claimed invention.

Conclusion

9. No claims are allowed.

10. Claims 1 and 5 are free of the prior art. The closest prior art is Roth, et al. (Nature Medicine, 1996, Vol. 2 No. 9, pages 985-991). Roth, et al. teach administration of a retroviral vector containing wild-type p53 to lung cancer patients (see Table 1). Roth, et al. do not teach nor reasonably suggest the use of clathrin heavy chains in combination with wild-type or mutated p53 to treat cancer.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571) 272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow

February 8, 2007

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER